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EXAMINER	
HELMS, LARRY RONALD	

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1642	18

DATE MAILED: 10/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/664,958	Applicant(s) TRAKHT ET AL.	
	Examiner Larry R. Helms	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) _____ is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 17+16.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Request for Continued Examination

1. The request filed on 7/30/03 for a Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 09/664958 is acceptable and a RCE has been established. Claims 6-7, 9, 16-18, 175-184 are pending and are currently under prosecution. An action on the RCE follows.

2. Claims 1-5, 8, 10-15 have been canceled.

Claims 6 and 16 have been amended and claims 175-184 have been added.

3. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.

4. The following Office Action contains NEW GROUNDS of rejection.

Rejections Withdrawn

5. The rejection of claims 6 and 16 under 35 U.S.C. 103(a) as being unpatentable over De Vries et al (PNAS 95:12340-12345, 1998) and Rousset et al (Oncogene 16:643-654, 1998) and as evidenced by the specification, and further in view of Campbell (Monoclonal antibody technology, Elsevier Science Publishers, pages 1-32, 1986) and Harlow et al (antibodies, A laboratory manual, Cold Spring Harbor Laboratory, page 322, 1988) and further in view of Adair et al (WO 91/09967, published 7/11/91) and Green et al (Nature genetics 7:13-21, 1994) is withdrawn in view that the

claims that contain the limitations needed in Adair and Green have been canceled and the 103 rejection below addresses the claim limitations of 6 and 16.

Response to Arguments/NEW GROUNDS of Rejection

6. The rejection of claims 6, 16 under 35 U.S.C. 103(a) as being unpatentable over De Vries et al (PNAS 95:12340-12345, 1998) and Rousset et al (Oncogene 16:643-654, 1998) and as evidenced by the specification, and further in view of Campbell (Monoclonal antibody technology, Elsevier Science Publishers, pages 1-32, 1986) and Harlow et al (antibodies, A laboratory manual, Cold Spring Harbor Laboratory, page 322, 1988) is maintained.

The response filed 7/30/03 has been carefully considured but is deemed not to be persuasive. The response states that the examiner has relied heavily on a generic statement in Cambell, page 29, that it is customary now for any group to clone the genes coding for a macromolecule and make monoclonal antibodies to it. The response states that by this logic (the examiners) the identification of a protein per se would necessarily preclude the antibody and the response cites in re Dual and consistent with Dual, applicants maintain that the teachings of a protein and a general approach to making antibodies cannot reasonably be construed as making obvious a monoclonal antibody that binds to a distinct domain (see page 18 of response). In response to this argument, the citation of Dual is concerned with a specific claimed DNA sequence which is not the case here and does not apply to these claims or its

interpretation. In view of the Campbell reference it is obvious to make a monoclonal antibody to TIP-2 and in fact it is obvious to make it to the "extracellular domain".

The response further states that although the TIP-2 is identified by De Vries et al and Rousset et al in 1998, the fact that , five years later, the examiner has not identified a teaching of TIP-2 antibodies produced by either De Vries or Rousset et al or by any one else other than applicants is at odds with the cited statements in Campbell and with the Examiners position (see page 18-19 of response). In response to this argument, the standard for a 103 rejection is obviousness not whether single references produce the claimed invention. The claims are rejected under 103 not 102 and as such a combination of references is used and combined. The requirement for 103 was stated in the office action mailed 9/26/02 and is repeated here

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The response further states that the term "domain" is a term in the art and the term means a peptide domain comprising less than the entire polypeptide and it is improper to refer to the entire protein as all of the domains and applicants not that the specification clearly indicates that 27.B1 and 27.F7 bind the extracellular and cytoplasmic domains, respectively of TIP-2 (see page 19 of response). In response to this argument, the term "domain" or "extracellular domain" is still indefinite and as such

can encompass any part of TIP-2 because the specification has not disclosed any amino acid sequence that is the "extracellular domain" or "cytoplasmic domain".

The rejection is maintained because both De Vries et al and Rousset et al specifically teach the PDZ domain of the TIP-2 antigen and its importance to its function and binding to other polypetides and it would have been obvious to make antibodies to these parts of the protein because this region is important for the interactions with other proteins and antibodies to this region can be used for monitering binding. The PDZ domain is identified in the prior art and due to the indefinite nature of the term "extracellular domain" and lacking a definition in the specification as to the amino acids that are encompassed by the phrase, an antibody to the PDZ domain meets the limitations of the claims. In addition the C terminus is also identified as being important in De Vries and Rousset et al and as such one would have motivation to make an antibody to this region because it is important to binding with other molecules. For the same reasons it would have been obvious to make an antibody to the PDZ domain it would also be obvious to make one to the C terminus. Although the claims require the TIP-2 to be on the surface of a tumor cell, it is obvious that the antibodies produced by the combination of references would bind to TIP-2 and since TIP-2 is on the surface of the tumor the antibodies would obviously bind and one would have a reasonable expectation of success that the antibodies bind to TIP-2 since that was the antigen that the antibodies were made against.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

7. The rejection of claims 6 and 16 and newly added claims 176-184 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained.

The response filed 7/30/03 has been carefully considured but is deemed not to be persuasive. The response states that "domain" is an art term that refers to a distinct structural or functional portion of a protein that comprises less than the entire polypeptide and a definition is supplied as "a discrete portion of a protein with its own function. The combination of domains in a single protein determines its overall function." and that "domain" refers to a structural or functional portion of the overall polypeptide (see page 21-22 of response). In response to this argument, the term "domain" or "extracellular domain" has not bee defined in term of the TIP-2 protein in the specification. The term "domain" may be a portion of the polypeptide, however, what region or amino acids are defined in the "extracellular domain". The specification does not define any specific region or if TIP-2 has an or "extracellular domain". Therefore one cannot determine the meets and bounds of the claims.

8. The rejection of claims 6 and 16 and newly added claims 176-184 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that

the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained.

The response filed 7/30/03 has been carefully considured but is deemed not to be persuasive. The response states that the term "domain" is used repeatedly in the specification and that the specification teaches 27.B1 binds an epitope of TIP-2 on the surface of breast cancer cells and 27.F7 binds a different epitope of tIP-2 that is intracellular and "though the specification does not explicitly state that the antibodies bind to different "domains", it would be clear to one skilled in the art that cell surface-associated TIP-2 protein contains at least an extracellular domain to which 27.B1 binds and an intracellular or cytoplasmic domain to which 27.F7 binds" (see page 23-24 of response). In response to this argument, while the specification does disclose the binding to the surface of cancer cells by 27.B1 and binding of 27.B7 intracellularly to fixed cells, there is nothing in the specification to define a "domain" or an "extracellular domain" or "intracellular domain". Therefore, the terms in the claims of "domain", extracellular domain" are new matter. Applicants are suggested to amend the claims to recite that 27.B1 binds to TIP-2 on the surface of cancer cells expressing TIP-2 and 27.F7 binds intracellularly to TIP-2 on fixed cells as recited in the specification on page 173, lines 22-25.

The following are some additional NEW GROUNDS of rejection

Claim Rejections - 35 USC § 112

9. Claim 16 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim has been amended to recite "binds the same extracellular domain of TIP-2 as does monoclonal antibody 27.F7". The response filed 7/30/03 states that support can be found for the limitation at pages 173, 175, 176. the response has been carefully considured but is deemed not to be persuasive. The recited pages show support for the 27.B1 antibody binding to TIP-2 on the surface of cancer cells, 27.F7 is stated to bind intracellularly to fixed cells. In addition the response states that 27.F7 binds to the cytoplasmic domain (see page 19 of response). Thus, it appears that there is no support for the clamed limitation. Applicants are required to point to specific support for the limitation in the specification as originally filed or remove it from the claim.

Claim Rejections - 35 USC § 103

10. Claims 175-180, 182-184 are rejected under 35 U.S.C. 103(a) as being unpatentable over De Vries et al (PNAS 95:12340-12345, 1998) and Rousset et al (Oncogene 16:643-654, 1998) and as evidenced by the specification, and further in view of Campbell (Monoclonal antibody technology, Elsevier Science Publishers, pages 1-32, 1986) and Harlow et al (antibodies, A laboratory manual, Cold Spring Harbor

Laboratory, page 322, 1988) and Adair et al (WO 91/09967, published 7/11/91) and Green et al (Nature genetics 7:13-21, 1994) and Wei et al (U.S. Patent 6,455,040, with priority to 5/99).

The claims recite a kit for detecting the TIP-2 cancer cells comprising a solid support with an anti-TIP-2 antibody that binds the same domain as 27.F7 or 27.B1 and a detectably labeled antibody labeled with a radioactive isotope, wherein the antibody is a monoclonal, humanized or human. For this rejection the intended use for detection of cancer cells is given no patentable weight.

De Vries et al and Rousset et al both teach the TIP-2 protein as evidenced from the specification at page 173-174. The protein of TIP-2 is also called GIPC which is taught by De Vries (see figure 1) and Rousset et al. De Vries et al and Rousset et la do not teach a monoclonal antibody to TIP-2 or a labeled antibody or a human or humanized antibody or a solid support with the antibody. These deficiencies are made up for by the teachings of Campbell, Harlow et al, Adair, Green, and Wei et al.

Campbell et al teach production of murine monoclonal antibodies.

Harlow et al teach labeling methods for detection.

Adair et al teach methods of humanizing antibodies comprising chimeric antibodies for human therapy and to prevent HAMA response.

Green et al teach human antibodies for lower immunogenicity in humans.

Wei et al teach methods of diagnosing using antibodies on a solid support and labeled antibodies and kits comprising such (see column 111).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced a kit comprising an antibody to TIP-2 which is a humanized or chimeric or human antibody to the protein of De Vries et al and Rousset et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced a kit comprising an antibody to TIP-2 which is a humanized or chimeric or human antibody to the protein of De Vries et al and Rousset et al because Rousset et al teach the TIP-2 protein interacts with the HTLV-1 Tax oncoprotein and the oncoprotein has been established to be associated with induction of tumors in transgenic mice (see page 643) and TIP-2 is a human protein that interacts with HTLV-1. In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced a kit comprising an antibody to TIP-2 which is a humanized or chimeric or human antibody to the protein of De Vries et al and Rousset et al because Green et al teach methods of producing human antibodies that reduce the immunogenicity when compared to mouse antibodies in treating human diseases. In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced a kit comprising an antibody to TIP-2 which is a humanized or chimeric or human antibody to the protein of De Vries et al and Rousset et al because Adair et al teach methods of humanized and methods comprising chimeric antibodies for therapy in humans to reduce the immunogenicity in humans compared to mouse antibodies. In addition, one of ordinary skill in the art would have been motivated to and had a reasonable

expectation of success to have produced a kit comprising an antibody to TIP-2 which is a humanized or chimeric or human antibody to the protein of De Vries et al and Rousset et al because Wei et al teach kits comprising solid supports with antibodies and assays for detection of antigens using the kits and labeled antibodies which is also taught by Harlow. Thus, since the TIP-2 protein is associated with an oncoprotein it would be obvious to produce a human, humanized, or chimeric antibody to the protein and produce a kit comprising the antibody on a solid support and a second labeled antibody.

Although the claim recites a kit, no positive recitation of the kit ingredients/elements distinguishes the claim over the references. Therefore, the references read on the claimed kit. Further, it is a well-known convention in the art to place the recited elements in a kit for the advantages of convenience and economy, and methods of detectably labeling antibodies and derivatives thereof also were well known and available to the ordinarily skilled artisan. Thus, the claimed subject matter is considered obvious over the prior art, absent sufficient factual evidence to the contrary.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

11. Claims 7, 9 and 17-18 are in condition for allowance. Claim 181 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in

independent form including all of the limitations of the base claim and any intervening claims.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

13. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242.

Respectfully,

Larry R. Helms Ph.D.

703-306-5879

LARRY R. HELMS, PH.D
PRIMARY EXAMINER